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EXAMINER	
SALMON, KATHERINE D	
ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,434	SIEMERING, VICTORIA ET AL.	
	Examiner	Art Unit	
	KATHERINE SALMON	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-47* is/are pending in the application.

4a) Of the above claim(s) *28-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to papers filed 10/07/2009.

2. Currently claims 26-47 are pending. Claims 1-25 have been cancelled.

3. Applicant has elected with traverse Claims 26-27 and the specific combination of connexin 26, pendrin, mitochondrial 12s rRNA and usherin and SEQ ID NO. 1 in the reply filed on 4/14/2009. As such, claims 28-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/14/2009.

Newly submitted claims 28-47 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Specifically the applicant was given an opportunity to elect a combination of Sequences which would include SEQ ID NO. 33-64 in the requirement for restriction of 3/30/2009. However, the applicant elected the search of SEQ ID No. 1. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 28-47 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

4. The following rejections for Claims 26-27 are necessitated by amendment. Response to arguments follows.

5. This action is FINAL.

Interview Summary

6. The reply filed on 10/07/2009 is a complete or accurate record of the substance of the phone interview of 8/10/2009.

Claim Amendments

7. The reply asserts that the newly added claims 28-47 are directed to the combination of SEQ ID NO. 33-64 (p. 7 2nd paragraph). The reply asserts that these claims correspond to the elected invention as these sequences are encompass by the elected combination of the four genes of connexin 26, pendrin, mitochondrial 12S rRNA and usherin (p. 7 last paragraph). The reply points to SEQ ID No. 33 which is included within the elected sequence of SEQ ID No. 1 (p. 8 1st paragraph). The reply asserts that therefore these claims should be included in the examination (p. 8 1st paragraph). The reply asserts that in event that the examiner considers the new claims to represent a nonelected invention that based upon the telephone interphone these claims would be considered upon filing of an RCE.

Response to arguments

As stated above, the applicant had the opportunity to elect a specific sequence or a specific combination of sequences in the requirement for restriction (dated 3/30/2009). The applicant, specific elected SEQ ID No. 1 and not the combination of SEQ ID No. 33-64. As such the restriction and the election of SEQ ID No. 1 is maintained. Although SEQ ID No 33 might be encompassed by the elected sequence of SEQ ID No.

1, the combination of SEQ ID NO. 33-64 is not encompassed by SEQ ID No. 1. Further the search of SEQ ID No. 1 would not provide art over the combination of SEQ ID No. 33-64 as this combination would include nucleic acid fragments not search by the search of SEQ ID No. 1. However, it is noted that the examiner did agree to a potential change in the elected invention at the time RCE.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kudo et al. (American Journal of Medical Genetics VOl. 90 p. 141) in view of Smith et al. (Seminars in Pediatric Neurology 2001 VOl 8 p. 147), Sato et al. (European Journal of Endocrinology 2001 VOl. 145 p. 697), Fischel-Ghodsian et al. (US Patent 5506101 April 9, 1996), Najera et al. (Human mutation June 2002 Vol. 20 p. 76 it is noted that for citation purposes the reference is numbers from p. 1-7), and Van Ness (US Patent

5994065 November 30, 1999).

With regard to Claims 26, Kudo et al teaches the genotyping of the connexin 26 gene for deafness by ASO hybridization (abstract). Kudo et al. teaches genomic DNA was examined by PCR and sequences using the ASO technique (p. 142 1st column last paragraph). Kudo et al. teaches that an allele specific probe on a membrane (e.g. a solid support) was contacted with DNA from connexion 26 (p. 143 1st column last paragraph). Kudo et al. teaches that the DNA was labeled with fluoreciein (e.g. a reporter label) to give a signal (p. 143 1st column last paragraph). Kudo et al. teaches hybridization such that the presence of absence of the reporter molecule can be screened to determine the genotype of the patient (p. 143 and Table II). Kudo et al. does not teach the specific hybridization constraints. Kudo et al. teaches the pathological condition was deafness (p. 142 1st paragraph).

However, Kudo et al. does not teach the specific hybridization constraints nor the genotyping of pendrin, mitochondrial 12s rRNA and usherin.

With regard to Claims 26, Smith et al. teaches that there are genes that are associated with sensorineural hearing loss (abstract). Smith et al. teaches that connexin 26 is the most common recessive nonsyndromic mutation of deafness (p. 151 1st column last paragraph). Smith et al. teaches that pendrin syndrome is characterized by a nonsyndromic locus DFNB4 (p. 152 2nd full paragraph). Smith et al. teaches mutations such as A1555G in the 12s RRNA gene is associated with nonsyndromic hearing loss (p. 156 2nd paragraph). Smith et al. teaches that usherin is a common defect for deafness (p. 149 2nd column 1st paragraph). Therefore Smith et al. teaches

connexion 26, pendrin, mitochondrial 12s rRNA and usherin are all associated with hearing loss.

With regard to Claims 26, Sato et al. teaches the detection of the missense mutation H723R in the pendrin gene is associated with hearing loss (abstract). Sato et al. teaches that PCR and then allele specific amplification was performed to genotype the mutation (p. 699 1st column 2nd paragraph). Sato et al. teaches that allele specific amplification was performed with wild type allele specific primers and a mutant allele specific primer (p. 699 1st column 2nd paragraph).

With regard to Claims 26, Fischel-Ghodsian et al. teaches a method of detecting 12s rRNA gene mutations associated with deafness (column 2 lines 32-36). Fischel-Ghodsian et al. teaches detection of the A1555G mutations as the 12S rRNA mutations associated with deafness (column 6 lines 50-56). Fischel-Ghodsian et al. teaches that an ASO hybridization technique can be performed to detect the mitochondrial mutations (column 4 lines 20-30).

With regard to Claims 26, Najera et al. teaches mutations of the usherin gene are associated with hearing loss (abstract). Najera et al. teaches that mutations in the usherin gene can be genotypes by performing a nucleic acid (p. 3 1st paragraph).

With regard to Claims 26, Van Ness teaches a method for hybridization which reduces the non specific background (abstract). Van Ness teaches a hybridization method which includes hybridization in the presence of 1X SSC at 42 degrees for 60 minutes (column 18 lines 13). Van Ness teaches the hybridization was followed by 4 washes of 1X SSC/0.1% SDS for 1 minute per wash (Column 18 lines 14-16). Van

Ness teaches that a final wash with 2X SSC and 0.1% Tween was used (Column 18 lines 14-17). Therefore Van Ness teaches the hybridization constraints of the instant claims.

Therefore it would be prima facie obvious to modify the method of Kudo et al. to further genotype the pendrin, mitochondrial 12s rRNA, and usherin genes as taught by Smith et al, Sato et al., Fischel Ghodsian et al, and Najera et al. using the hybridization constraints of Van Ness. The ordinary artisan would be motivated to genotype all of these genes because Smith et al. teaches that all of these genes are associated with hearing loss. Therefore the ordinary artisan would be motivated to detect all mutations involved in hearing loss including the mutations of pendrin, mitochondrial 12s rRNA, and usherin as taught by Sato et al, Fischel Ghodsian et al, and Najera et al. using the ASO method of Kudo et al. One of ordinary skill in the art would have been motivated to genotype the known genes of connexion 26, pendrin, mitochondrial 12s rRNA and usherin by applying the conventional methodology of ASO hybridization. The ordinary artisan would be motivated to perform routine optimization of the method of Kudo et al. and use the hybridization constraints of Van Ness in order to reduce hybridization backgrounds with a predictable expectation of successful hybridization due to the functional similarities of the washing conditions of Kudo et al. and Van Ness.

Response to Arguments

The reply traverses the rejection. A summary of the arguments made in the amendment are summarized below with response to arguments following.

The reply asserts that the claim as amended is direct to genotyping a subject using hybridization with a panel of ASOs covering a mutation of each of the 4 specific probes (p. 9 last paragraph). The reply asserts that the key feature of the claimed method is a method to genotype 4 genes simultaneously using an array under a single set of hybridization conditions (p. 9 last paragraph). The reply asserts that the ability to detect multiple mutations in a single hybridization assay in an array format is demonstrated in Example 6 and 7 of the instant specification (p. 10 1st full paragraph). The reply asserts that although the references teaches the association of the 4 genes to hearing loss, the references do not teach a method which is capable of determining mutations in all 4 genes using a single test (p. 10 2nd full paragraph). The reply asserts that the cited references use different methodologies for detecting such that Kudo and Fischel-Ghodsian teach ASO, Sato allele specific PCR, Najera teaches SSCP, and Smith et al only provides a discussion of genes and mutations associated with hearing loss (p. 10 3rd full paragraph). The reply asserts that therefore the combined references do not devise a single array hybridization test in order to detect mutations in all 4 genes and there would not have been any reasonable expectation of success of devising a single array hybridization test (p. 10 last paragraph).

These arguments have been fully reviewed but have not been found persuasive.

It is noted that the method is drawn to contacting a panel of ASO probes on a support which represents genes connexion 26, pendrin, mitochondrial 12s rRNA, and usherin with a hybridization solution to determine hybridization to a target. This analysis of multiple probes on a single support is well known in the art. Further Kudo et al

teaches that probes on a membrane can be contacted in the presence of a hybridization solution to a target. Although Kudo et al. does not teaches the specific hybridization solution used, Van Ness et al. teaches hybridization solution of the instant claims can be used to reduce the nonspecific background noise.

The reply asserts that the key feature is the analysis of 4 different genes on a hybridization support; however, the reply has not brought any evidence that such an analysis would be unexpected at the time of filing. Further it is noted both the ASO hybridization technique and the correlation of the elected genes to deafness was known at the time of filing (as shown by the art of the 35 USC 103(a) rejection presented above. As such although the art at the time of filing does not teach an ASO hybridization assay with the elected 4 genes, it would be obvious to one of ordinary skill in the art based upon the teaching of the art used in the 35 USC 103(a) to detect mutations in each gene using an ASO hybridization technique of Kudo et al. with the predictable expectation of successful hybridization to targets genes associated with hearing loss.

The reply asserts that not all of the cited references teach the use of ASO probes for the mutations in the recited genes. However, the analysis of know areas of mutation by ASO hybridization techniques is well known in the art. The ordinary artisan would have a reasonable expectation of success of taking any of the mutations listed in Smith et al, Sato et al, Fischel Ghodsian et al and using these mutations in a ASO hybridization technique of Kudo et al. with predictable expectation of successfully hybridization mutations found within each of these genes with samples which include

targets that have those specific mutations. Although the cited references use different hybridization techniques to detect these mutations, the reply has not provided any arguments that these mutations would not be detected using an ASO methodology of Kudo et al.

10. Claim 27 is rejected over Kudo et al. (American Journal of Medical Genetics VOl. 90 p. 141),Smith et al. (Seminars in Pediatric Neurology 2001 VOl 8 p. 147), Sato et al. (European Journal of Endocrinology 2001 VOl. 145 p. 697), Fischel-Ghodsian et al. (US Patent 5506101 April 9, 1996), Najera et al. (Human mutation June 2002 Vol. 20 p. 76 it is noted that for citation purposes the reference is numbers from p. 1-7), and Van Ness (US Patent 5994065 November 30, 1999) as applied to claims 1-12, 17, and 26 and further in view of Dobrowolski et al. (2004/0038266 February 26, 2004).

Although the combination of Kudo et al, Smith et al., Sato et al, Fischel-Ghodsian et al, Najera et al. and Van Ness teach a method for genotyping a subject for connexin 26, pendrin, mitochondrial 12s rRNA, and usherin, the combination does not teach a method of genotyping connexin 26 wherein the oligonucleotide comprises SEQ ID No. 1.

With regard to Claim 27, Dobrowolski et al. teaches a method of screening for hearing loss by detection of connexin 26 mutations. Dobrowolski et al. teaches a method of detecting connexin 26 mutations using the sequence of SEQ ID No. 1 (p. 2 paragraph 19). Dobrowolski et al.'s Seq id no. 1 comprises the instantly claimed SEQ

ID No. 1 (see alignment below) and therefore the genotyping of the connexin mutation in Dobrowolski et al by the methodology of Kudo et al, Smith et al., Sato et al, Fischel-Ghodsian et al, Najera et al. and Van Ness would produce a oligonucleotide which comprises SEQ ID No. 1.

```
Query Match          100.0%;  Score 28;  DB 46;  Length 28;
 Score over Length    100.0%;
 Best Local Similarity  100.0%;  Pred. No. 0.95;
 Matches  28;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

Qy              1  TTTTTTTTTTGATCCTGGGGGGTGTGAA  28
                   ||||||||||||||||||||||||||||
Db              1  TTTTTTTTTTGATCCTGGGGGGTGTGAA  28
```

Therefore it would be prima facie obvious to one of ordinary skill in the art at the time of filing to modify the method of Kudo et al, Smith et al., Sato et al, Fischel-Ghodsian et al, Najera et al. and Van Ness to detect any number of connexin mutations, including the mutation of Dobrowolski et al. using the oligonucleotide comprising SEQ ID No. 1 with a reasonable expectation of success. It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply a known ASO hybridization technique use to detect connexin mutations to further genotype other connexin mutations including those represented by SEQ ID No. 1 with the predictable expectation that the connexion 26 mutation will be genotyped.

Response to Arguments

The reply traverses the rejection. A summary of the arguments made in the amendment are summarized below with response to arguments following.

The reply asserts that the combination of Kudo et al., Smith et al, Sato, Fischel-Ghodsian, Najera, and Van Ness does not teaches the recited features of the independent claim 26 (p. 11 last paragraph).

This argument has been fully reviewed but has not been found persuasive.

As discussed in the response to arguments above, it is the examiners position that the combination of Kudo et al., Smith et al, Sato, Fischel-Ghodsian, Najera, and Van Ness teach all the recited limitations of Claim 26. As such the combination in view of Dobrowolski is maintained.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to KATHERINE SALMON whose telephone number is (571)272-3316. The examiner can normally be reached on Monday - Friday 9AM-530PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Katherine Salmon

/Sarae Bausch/
Primary Examiner, Art Unit 1634